



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2018-D-3903]

Chronic Hepatitis B Virus Infection: Developing Drugs for Treatment; Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a final guidance for industry entitled “Chronic Hepatitis B Virus Infection: Developing Drugs for Treatment.” The purpose of this guidance is to assist sponsors in the clinical development of drugs and biologics for the treatment of chronic hepatitis B virus (HBV) infection from the initial investigational new drug application (IND) through the new drug application (NDA)/biologics license application (BLA) and postmarketing phases. This guidance finalizes the draft guidance of the same title issued on November 2, 2018.

DATES: The announcement of the guidance is published in the *Federal Register* on [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

ADDRESSES: You may submit either electronic or written comments on Agency guidances at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be

posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.

- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2018-D-3903 for "Chronic Hepatitis B Virus Infection: Developing Drugs for Treatment." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy,

including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA’s posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at:

<https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT: Poonam Mishra, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 6100, Silver Spring, MD 20993, 301-796-1500.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a final guidance for industry entitled “Chronic Hepatitis B Virus Infection: Developing Drugs for Treatment.” The purpose of this guidance is to provide general recommendations on the clinical development of drugs and biologics for the treatment of chronic HBV infection from the initial IND through the NDA/BLA and postmarketing phases. The guidance includes general considerations for nonclinical toxicology and virology studies, early phase clinical development, clinical pharmacology assessments, and phase 3 safety and efficacy trials. The guidance discusses phase 3 trial design considerations and efficacy endpoints for the development of finite duration therapies for the treatment of chronic HBV infection. Drug development considerations for specific subpopulations such as patients co-infected with hepatitis D virus or human immunodeficiency virus and for pediatric patients with chronic HBV infection are also included.

This guidance finalizes the draft guidance of the same name issued on November 2, 2018 (83 FR 55187). FDA provided clarifying edits to the final guidance and included additional information after considering comments received on the draft guidance. Changes from the draft to the final guidance include the following: considerations and recommendations for studies evaluating oligonucleotide-based investigational drugs, considerations for drugs developed to modulate innate and adaptive immune responses, updates to trial design considerations, updates to recommendations for safety monitoring (including monitoring for hepatitis flares after treatment discontinuation), and updates to efficacy extrapolation from adult to pediatric patients.

This guidance is being issued consistent with FDA’s good guidance practices regulation (21 CFR 10.115). The guidance represents the current thinking of FDA on “Chronic Hepatitis B Virus Infection: Developing Drugs for Treatment.” It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521) is not required for this guidance. The previously approved collections of information are subject to review by OMB under the PRA. The collections of information for review of investigational new drug regulations in 21 CFR part 312 have been approved under OMB control number 0910-0014, and the collections of information for review of new drug applications and biologic license applications in 21 CFR parts 314 and 601, have been approved under OMB control numbers 0910-0001 and 0910-0338, respectively. The collection of information regarding accelerated approval of serious conditions for drugs and biologics is approved under OMB control number 0910-0765. The collection of information regarding labeling of prescription drug and biologic products is approved under OMB control number 0910-0572.

III. Electronic Access

Persons with access to the internet may obtain the guidance at <https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs>, <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>, or <https://www.regulations.gov>.

Dated: April 1, 2022.

Lauren K. Roth,

Associate Commissioner for Policy.